

***REMARKS*****Newly Added Claims**

Claims 17 and 18 are newly added herein. Support for the newly added claims can be found throughout the originally-filed specification, and in particular at least at the following passages: pages 12-17, 21-25, *et seq.* and FIGs. 1A, 1B, and 2.

**Cancellation of Claims**

Claims 15-16 are canceled without prejudice, waiver, or disclaimer. Applicant takes this action merely to reduce the number of disputed issues and to facilitate early allowance and issuance of other claims in the present application. Applicant reserves the right to pursue the subject matter of these canceled claims in a continuing application, if Applicant so chooses, and does not intend to dedicate any of the canceled subject matter to the public.

**Specification Objections**

1. Applicant has changed the trademark TRITON X-100 to be capitalized throughout the specification, has indicated the registered trademark status of the mark TRITON with the “®” designation, and has followed the term “TRITON® X-100” with the generic terminology “surfactant.”
  
2. The specification is objected to because documents have allegedly been improperly incorporated certain documents by reference. Applicant respectfully traverses the rejection.

Incorporation of material by reference into a patent application is permissible. *Ex parte Schwarze*, 151 USPQ 426 (Bd. App. 1966); *see also* MPEP § 608.01(p). The Office Action cites *In re de Seversky*, 474 F.2d 671, 177 USPQ 144 (CCPA 1973) for the proposition that the “[m]ere reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure required by 35 U.S.C. 112, first paragraph.” Applicant respectfully submits that the Office Action misapplies *Seversky*.

In *Seversky* the patent at issue did not contain the phrase “incorporation-by-reference” anywhere in the specification, and the patentee attempted to argue that material from the parent application was incorporated into the patent at issue by virtue of the statement that the application for the patent was a “continuation-in-part” of the parent. *Id.* The Court noted that

the statement that the patent was a continuation-in-part does not operate to incorporate in an application any part of the disclosure of the parent application so referred to.

Thus, *Seversky* is distinguishable because here, unlike the patent in *Seversky*, Applicant has specifically used the language “incorporated-by-reference.”

The Office Action further quotes the following language from the MPEP 608.01(p)I: In addition to other requirements for an application, the referencing application should include an identification of the referenced patent, application, or publication. Particular attention should be directed to specific portions of the referenced document where the subject matter being incorporated may be found.

Applicant respectfully asserts that it has complied with this suggestion by the MPEP. First, the application has included very clear identifications of the references that are incorporated, including a detailed cite to each reference, including the pages at which the reference may be found in a particular publication. Second, Applicant has amended the specification herein to indicate that the application includes the references “in their entireties.” Applicant submits that the addition of this phrase indicates specifically where the subject matter being incorporated may be found. Additionally, the incorporation by reference of entire documents is extremely common practice in patent drafting.

The one exception is for the reference to “Molecular Cloning, A Laboratory Manual” on page 34, where the specification has been amended to indicated that only the passages relating to PCR are incorporated by reference because of the extensive nature of this work. Applicant believes that quick reference to the Index of said Manual will direct one easily to the relevant passages that are incorporated by reference.

Because the Applicant used the language “incorporated by reference” in the original specification, and the specification has been amended to incorporate the references “in their entirety”, and because *Seversky* is misapplied, Applicant respectfully submits that the objection should be withdrawn.

The omnibus incorporation by reference appearing on page 40 has been deleted by the amendment made to the specification above. Applicant respectfully submits this objection has now been rendered moot.

#### **Claim Rejections under 35 U.S.C. § 112**

1. Claims 10-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicant respectfully traverses the rejections and

asserts that there is support throughout the specification as originally filed for claims 10-14, particularly at pages 15-17 for the definitions of "label" and "signal producing system" and at page 21, lines 4-11 relating to determining sequences of nucleic acids. The originally-filed specification does convey to one skilled in the art that Applicant had possession of the subject matter of claims 1-10. Nevertheless, to advance prosecution, Applicant has amended claim 10 herein as follows:

by detecting a label that is part of the nucleic acids chosen from at least one of: the biological sample and the second plurality of nucleic acids;  
g) determining a position on the substrate of the detectable signal of the label; and  
g h) determining the sequence of the nucleic acid in the biological sample that has hybridized to a nucleic acid of the second plurality by correlating the position of the signal to the sequence.

*Claim 10*, as amended, in part.

Thus, the Office Action's assertion that "Claim 10 has also been interpreted as encompassing said sequence determination when no label or detection means are employed" no longer applies. *Office Action* at 6.

The Office Action further alleges the following:

A review of the disclosure finds but two examples....

As plainly evident above, none of these examples describes the claimed method of sequencing any nucleic acid.

While the specification has been found to contain forward-looking statements as to how a method of sequencing nucleic acids could possibly be conducted, the specification has not been found to provide the requisite written description of the claimed invention in such full, clear, and concise language so as to reasonably suggest that applicant was in possession of the invention at the time of filing. It appears that application is attempting to satisfy the written description requirement...though obviousness.

*Office Action* at 7. Applicants respectfully traverse this rejection.

There is clear support throughout the originally-filed specification for the recited features/steps of amended claim 10 for determining the sequence of the nucleic acid in the biological sample plurality by correlating the position of a signal from a label to the sequence. Support can be found in the originally-filed specification for the recited features/steps of sequencing using a label, detecting the label, and from the position of the detected label,

determining the sequence of the nucleic acid in the biological sample by correlating the position of the detected label to the sequence.

The explanations of the terms "substrate or surface," "label," and "signal producing system," including what they are, and how they are used to determine the sequence of a nucleic acid in a sample are clearly set forth in the "Definitions" section of the specification at pages 14-17. Portions are reproduced here below:

"Label": A label as used herein means to a member of a signal producing system. Usually the label is part of a target nucleotide sequence or an oligonucleotide probe, either being conjugated thereto or otherwise bound thereto or associated therewith. The label is capable of being detected directly or indirectly. Labels include (i) reporter molecules that can be detected directly by virtue of generating a signal, (ii) specific binding pair members that may be detected indirectly by subsequent binding to a cognate that contains a reporter molecule, (iii) oligonucleotide primers that can provide a template for amplification or ligation or (iv) a specific polynucleotide sequence or recognition sequence that can act as a ligand such as for a repressor protein, wherein in the latter two instances the oligonucleotide primer or repressor protein will have, or be capable of having, a reporter molecule. In general, any reporter molecule that is detectable can be used....

The label can generate a detectable signal either alone or together with other members of the signal producing system. As mentioned above, a reporter molecule can be bound directly to a nucleotide sequence or can become bound thereto by being bound to an specific binding pair (sbp) member complementary to an sbp member that is bound to a nucleotide sequence. Examples of particular labels or reporter molecules and their detection can be found in U. S. Patent No. 5,508,178, the relevant disclosure of which is incorporated herein by reference. When a reporter molecule is not conjugated to a nucleotide sequence, the reporter molecule may be bound to an sbp member complementary to an sbp member that is bound to or part of a nucleotide sequence.

"Signal Producing System": A signal producing system as used herein means to a system that generates a *signal that typically relates to the presence or amount of a target polynucleotide in a medium*. A signal producing system may be incorporated on the oligonucleotide probes and relates to the presence of probes in a medium. The signal producing system includes all of the reagents required to produce a measurable signal. Other components of the signal producing system may be included in the developer solution and can include substrates, enhancers, activators, chemiluminescent compounds, cofactors, inhibitors, scavengers, metal ions, specific binding substances required for binding of signal generating substances, and the like. Other components of the signal producing system may be coenzymes, substances that react with enzymic products, other enzymes and catalysts, and the like. The signal producing system provides a signal detectable by external means, by use of electromagnetic radiation, desirably by optical examination. Signal-producing systems that may be employed in the present

invention are those described more fully in U.S. Patent No. 5,508,178, the relevant disclosure of which is incorporated herein by reference in its entirety.

*Specification at 15-17 (emphasis added).*

Using the position of the signal detected to correlate the signal to the sequence is also clearly explained in the specification. For example, the specification teaches that:

In particular after hybridizing to probes on the array, *the position and amounts of the target nucleic acids are determined using a signal molecule (e.g. radioactive, fluorescent, chemiluminescent). By determining the position of the signal on the array and correlating the position to the sequence of the oligonucleotides, information on the sequences of nucleic acid and the amounts in the sample is determined.*

*Specification at 21 (emphasis added).*

Therefore, because the specification does describe in full, clear, and concise language so as to reasonably suggest that applicant was in possession of the invention at the time of filing the method of sequencing the nucleic acid, Applicant submits that claims 10-14 do meet the written description requirement. Therefore, Applicant respectfully requests that the rejection be withdrawn.

2. Claims 10-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because “one cannot enable that which they do not yet possess.” *Office Action* at 9. Applicant respectfully traverses the rejections and asserts that because there is adequate written description, as described above, there is also enablement of claims 10-14. Therefore Applicant respectfully requests that the rejection be withdrawn.

**CONCLUSION**

In light of the foregoing amendments and for at least the reasons set forth above, Applicant respectfully submits that all rejections have been traversed, rendered moot, and/or accommodated, and that the now pending claims 10-14 and 17-18 are in condition for allowance. Favorable reconsideration and allowance of the present application and all pending claims are hereby courteously requested. If, in the opinion of the Examiner, a telephonic conference would expedite the examination of this matter, the Examiner is invited to call the undersigned agent at (770) 933-9500.

Respectfully submitted,

  
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